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Effects of dopaminergic medication on reactive and proactive inhibitory control

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Objective: In this study, we addressed the effects of dopaminergic treatment (DT) on the two domains of motor inhibition, i.e., reactive (the ability to react to a stop signal) and proactive inhibition (the ability to adapt the motor strategies according to the current context flexibly) according to the stage of Parkinson's disease (PD).

Methods: We recruited cognitively unimpaired PD patients under DT in the early (H&Y 1/1.5, n=20), intermediate (H&Y 2, n=20), and moderate/advanced (H&Y 2.5/3, n=20) stages and 30 age-matched healthy controls. Each participant underwent a standardized motor and cognitive assessment and stop-signal task (SST). Covariance analyses adjusted for the effect of age, sex, and UPDRS3 evaluated the differences between the performance in the SST (in terms of reactive and proactive inhibition) in DT ON and OFF and each stage of the disease as well as in comparison with controls.

Results: We found that reactive and proactive inhibition are progressively impaired along the disease. However, DT negatively affects reactive inhibition in the early and proactive inhibition in the intermediate PD stage. By contrast, DT does not impact motor inhibition in H&Y 2.5/3 patients. Relevantly, these effects are not only generated by the administration of dopamine agonists but also by L-Dopa.

Conclusions: In PD's early and intermediate stages, the DT negatively impacts reactive and proactive inhibition, respectively, despite improving motor symptoms. Such evidence supports the dopamine overdose hypothesis [1], which suggests that the administration of DT in the first stages of PD benefits dopamine-depleted dorsal striatal circuitries improving motor symptoms but overdose the more intact dopamine-dependent circuitries of the ventral striatum, impairing executive functions relying on it. Such findings suggest that the DT has to be titrated carefully to maximize patients' quality of life in the first stages of PD.

References:

[1] Vaillancourt et al (2013) Mov Disord. 28:1920-9.